UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/547,995	10/28/2005	David John Grainger	50461/003001	8214

21559 7590 05/27/2008

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
05/27/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/547,995	GRAINGER, DAVID JOHN	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-12,14-40,45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-21 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/7/05;12/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 13-21 and 41-44 in the reply filed on 1/31/08 is acknowledged.

Status of the Claims

Claims 1-46 are pending.

Claims 1-12, 14-40 and 45-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 13-21 and 41-44 are under examination.

Information Disclosure Statement

The information disclosure statement filed 9/7/2005 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has

been placed in the application file, but the information referred to therein has not been considered.

Applicants state that the references are listed in the enclosed Form PTO-1449 with the enclosed copies of the references. However, form PTO 1449 is not evident on file.

Specification

The abstract of the disclosure is objected to because it uses the PCT abstract. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's

cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-21 and 41-44 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed mixtures of peptides comprising of the naturally occurring amino acid residues read on naturally occurring peptides comprising of different amino acids of the native residues that formed different types of peptides. Also, the claimed library lacks patentable utility. It is not readily apparent from the disclosure the utility of a mere collection of known peptides comprising of the naturally occurring amino acid residues. Virtually all peptides in nature are comprised or made up of the 20 natural amino acids. There is no novelty in simply compiling or collecting these known compounds. If it is useful as a screening tool, then the method using the known compounds are more appropriate.

The court in Brenner v. Manson, 148 U.S.P.Q. 689 (1966),expressed the opinion that all chemical compounds are “useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of useful" as it appears in 35 U.S.C. §I01, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The Court held that: The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility .... [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field .... a patent is not a hunting license .... [i]t is not a reward for the search, but compensation for its successful conclusion. Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner, 148 USPQ at 696.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A). Claims 13-21 and 41-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antigenic amino acids selected from: GROUP 1 (charged) Arg, Lys, His, Asp, Gin; GROUP 2 (small hydrophobic) Gly, Ala, Leu, Ile, Val; GROUP 3 (large hydrophobic) Met, Phe, Pro, Tyr, Trp and GROUP 4 (hydrophilic) 8er, Thr, Asn, Gin, Cys (see e.g., page 55), does not reasonably provide enablement for X as groups of amino acid consisting of less than 20 different amino acids The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification fails to teach how to make and use the claimed broad mixtures of peptides or library of mixtures wherein each of the amino acids in the mixtures comprised any of number of groups of amino acids. The claimed number of groups would encompass a huge combination of different amino acids in a group hence, a potentially huge numbers of mixtures of peptides. The specification recites the specific groups of e.g., hydrophobic amino acids. However, the claimed groupings do not fall within

the disclosed groups. Because peptide sequence hence, its conformation dictates the function of the peptide hence, it is not clearly apparent from the huge scope of the claims the ones that would result in a peptide having a function. Neither does it disclose a library that can be screened for a particular purpose/function. The high unpredictability in the peptide art is notoriously known in the art. The art is inherently unpredictable because it is not possible to predict which predetermined (variations) of amino acids would result in the desired mutant with a desired binding function. It is generally known that the conformational freedom that promotes binding, e.g., by modifying the peptides, might be restricted which may likely perturb the function and stability of the peptide (protein) in ways difficult to predict and measure. Some peptides accommodate variations at numerous sites throughout their primary sequence. Others are much less accommodating. It is difficult in general to predict which peptides are robust to variations, and which sites in a particular peptide are best suited to variations of multiple independent sequences. The complex spatial configuration of amino acid side chains in peptides and the interrelationship of different side chains in the randomized sites are insufficiently understood to allow for such predictions. Each of the 19 amino acids is integrated at different frequencies due to the

degeneration of the genetic code. For instance, serine is integrated six times more often than tryptophan, and three times more often than aspartic acid. It would therefore require an enormous effort to isolate mutants corresponding to amino acids represented only once or twice. Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined molecule in a peptide mixture that would result in a mutations having function without undue experimentation. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

B). Claims 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 44 which describes the kit as comprising of the peptide of the given formula and a labeled antibody is not

supported in the as-filed specification. Likewise, claim 43, which recites a kit comprising antibodies specific to two or more immunoglobulin subclasses is not supported in the original disclosure. MPEP 714.02 clearly states that applicants specifically point where in the specification support for the newly added limitations appear.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-21 and 41-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 13 drawn to a mixture of peptides is but the library of claim 18. Therefore, these claims are duplicates.

2. Claim 13 is unclear in the recitation that “each group of amino acids consists of less than 20 different amino acid”. This is inconsistent with the recitation that “ all of the following amino acids are present in at least one

group: arginine, lysine and etc. Furthermore, if all peptides are of the same length and at least one group contains all of the 20 amino acids then it is not clear as to the sequence of the other groups.

3. In claim 3 the claimed "for each peptide in the mixture the amino acid at the same position is selected from the same group" is confusing, especially in the absence of positive recitation of the groups. Given no structure it is unclear which position is being referred thereto.

4. Claim 41 is unclear as to the binding of antibodies to immnoglobulins. Is it to antigen which is positively recited in (i) or to immunoglobulins of no antecedent basis? Clarification/explanation is required. Also, it is not clear as to the differentiating characteristics of a plurality or mixtures of antigens.

5. Claim 42 is unclear as to when the plurality of antigens comprises alternatively as an oligopeptide alone or together in combination with oligosaccharides.

6. Claim 44 improperly depends on non-elected method claim.

7. Claims 41-44 is indefinite as to the components of a kit such that the kit can be used for the intended purpose e.g., instructions as to the use of the kit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 13-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Houghten et al (Nature, 1991) or Devlin (Science).

Houghten et al discloses, throughout the article, at e.g., page 84 a mixtures of peptides and the heterogeneous libraries formed from the mixtures. The mixtures of peptide or library of hexapeptides comprises the formula as shown at Table 1, page 84, col. 2. See also, Fig. 1 at page 85 and Table 2 at page 86. Therefore, the specific mixtures of Houghten which describes specific residues fully meet the broad claimed mixtures/libraries with no defined structures or sequences.

Devlin discloses throughout the article, at e.g., page 404 a library of peptide encoded by nucleic acid having formula (NNS) which encodes all 20 amino acids. See further page 405, Table 2.

Devlin which describes specific residues fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

Claims 13-21 and 41-44 are rejected under 35 U.S.C. 102(e) as being anticipated by Fowlkes et al (USP 6617114).

Fowlkes et al disclose throughout the patent, at e.g., col.16, line 46 up to col. 18, line 16:

> A peptide library is a combinatorial library, at least some of whose members are peptides having three or more amino acids connected via peptide bonds. In an oligopeptide library, the lengths of the peptides do not exceed 50 amino acids. The peptides may be linear, branched, or cyclic, and

may include nonpeptidyl moieties. The amino acids are not limited to the naturally occurring amino acids.
A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues. The individual members are referred to as peptide ligands (PL). In one embodiment, an internal residue is constant, so that the peptide sequence may be written as (Xaa)m-AA1-(Xaa)n…
Where Xaa is either any naturally occurring amino acid, or any amino acid except cysteine, m and n are chosen independently from the range of 2 to 20, the Xaa may be the same or different, and AA1 is the same naturally occurring amino acid for all peptides in the library but may be any amino acid. Preferably, m and n are chosen independently from the range of 4 to 9.
Preferably, AA1 is located at or near the center of the peptide. More preferably, AA1 is either (a) at least five residues from both ends of the peptide, or (b) is in the middle 50% of the peptide. More preferably, that m and n are not different by more than 2; most preferably m and n are equal. Even if the chosen AA1 is required (or at least permissive) of the TP binding activity one may need particular flanking residues to assure that it is properly positioned. If AA1 is more or less centrally located, the library presents numerous alternative choices for the flanking residues. If AA1 is at an end, this flexibility is diminished. The most preferred libraries are those in which AA1 is tryptophan, proline or tyrosine. Second most preferred are those in which AA1 is phenylalanine, histidine, arginine, aspartate, leucine or isoleucine. Third most preferred are those in which AA is asparagine, serine, alanine or methionine. The least preferred choices are cysteine and glycine. These preferences are based on evaluation of the results of screening random peptide libraries for binding to many different TPs.
See further all the Examples which describe the specifics of the library containing tags.

Claims 41-44 drawn to a kit is disclosed at col. 31, line 15.

Fowlkes which describes specific residues for the library fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

Claims 13-21 and 41-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Lynch et al (5962244).

Lynch discloses throughout the patent at e.g., col. 13, line 13 up to col. 14, line 67:

> A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis, by combining a number of chemical "building blocks," such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide library, is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.
>
> Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (see, e.g., U.S. Pat. No. 5,010,175, Furka, Int. J. Pept. Prot. Res., 37:487-493 (1991) and Houghton, et al., Nature, 354:84-88 (1991)). Other chemistries for generating chemical diversity libraries can also be used.
>
> The invention provides compositions, kits and integrated systems for practicing the assays described herein. For example, an assay composition having a peptidyl-tRNA analog, an aminoacyl-tRNA analog, an immobilizable tag bound to the peptidyl-tRNA analog and a label bound to the aminoacyl-tRNA analog is provided by the present invention.

> The invention also provides kits for practicing the peptidyl transferase screening assays described above. The kits can include any of the compositions noted above, and optionally further include additional components such as instructions to practice a high-throughput method of screening for a peptidyl transferase activity modulator, one or more containers or compartments (e.g., to hold peptidyl-tRNA analogs, uninoacyl-tRNA analogs, modulators, or the like), a control activity modulator, a robotic armature for mixing kit components, and the like.

Lynch which describes specific residues for the library fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

Claims 13-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al(5858670).

Lam discloses throughout the patent at e.g., col. 3, line 14 up to col. 7, line 10:

> The present invention is directed to a library of bio-oligomers comprising all possible combinations of subunits…..FIG. 1. Scheme for random peptide synthesis using the split synthesis method for a random tripeptide with a terminal tryptophan added: X-X-X-W (wherein X=S, A, or V; there are 3.sup.3, or 27, possibilities).

> In specific examples, infra, enzyme-chromogen labels and fluorescent (FITC) labels are used.

Lam which describes specific residues for the library fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/T. D. Wessendorf/

Primary Examiner, Art Unit 1639

May 8, 2008